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EXAMINER	
GANGLE, BRIAN J	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,618	KINTRUP ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *4,14-18,20,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-13,19,21-23 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/5/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and remarks, filed on 5/5/2008, are acknowledged. Claims 2-15 and 18-19 are amended. Claims 21-30 are added. Claims 1-30 are pending. Claims 4, 14-18, 20, and 24-25 are withdrawn as being drawn to nonelected inventions. Claims 1-3, 5-13, 19, 21-23, and 26-30 are currently under examination.

Election/Restrictions

Applicant continues to argue the restriction requirement.

1. Applicant states that the examiner has cited new combinations of documents support the restriction and applicant has had no opportunity to respond; thus the finality of the restriction is premature.

2. Applicant argues that West does not teach a test system with cardiolipin antigens provided on a carrier and that the product inserts from Omega and Becton Dickinson are unsuitable to prove that the RPR test from Quorum diagnostics employs a cardiolipin antigen on a carrier.

3. Applicant argues that the "reagin" employed in RPR tests is not a coal carrier on which the antigen is immobilized, but rather, a suspension of VDRL particles and charcoal particles. Applicant asserts that "the coal particles just increase the absorptivity of the formed antigen-antibody complex by causing a 'flocculation'."

4. Applicant argues that there is no prior art suggesting a test which employs both a Treponema antigen as well as a cardiolipin antigen on a single carrier.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, the basis for the finding of unity has not changed and no new grounds for this finding have been set forth. The new documents cited were used as evidence to rebut applicant's assertions regarding the teachings of West.

Regarding argument 2, Quorum diagnostics is a subsidiary or Omega; thus the product insert from Omega is highly appropriate to show the contents of the RPR test. The test from Becton Dickinson was used to show that other RPR tests contain the same antigen. Product inserts from other companies bear out the fact that the RPR test contains immobilized cardiolipin. The ASI RPR test card product insert states, "the reagin-type antibody binds with

the antigen that is composed of a complex of cardiolipin, lecithin and cholesterol particles with activated charcoal" (see section 3, Principle of the Procedure). The product insert from Weiner Labs RPR test states, "In the rapid test for plasmatic reagins (RPR) the "reagins" present in individuals infected with *T. pallidum* are detected by their reaction to a cardiolipin antigen, lecithin and cholesterol adsorbed onto charcoal particles" (under PRINCIPLE, page 1).

Regarding argument 3, RPR tests do not contain "reagin," they are used to detect "reagin." Reagin is what binds to the antigen present in the test kit. The BD RPR test insert states that the "RPR Card antigen suspension is a carbon particle cardiolipin antigen." One does not generally refer to *an* antigen when they are referring to multiple molecules that are simply in suspension with each other. However, even if the cardiolipin were not bound to the charcoal before mixing the particles in suspension, charcoal is known to adsorb cardiolipin, lecithin, and cholesterol. Mixing VDRL antigen in suspension with charcoal particles would result in VDRL that is adsorbed to the charcoal.

Regarding argument 4, prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art. The prior art reference (or references when combined) need not teach or suggest all the claim limitations.

Applicant is reminded that the restriction requirement has been made final and will not be addressed again.

Information Disclosure Statement

The information disclosure statement, filed on 5/5/2008, has been considered. An initialed copy is enclosed.

Objections Withdrawn

The objection to claims 2 and 13 because the claims contain the acronym VDRL, is withdrawn in light of applicant's amendment thereto.

The objection to claims 5, 10, and 13 because the claims contain confusing Markush language, is withdrawn in light of applicant's amendment thereto.

Objections Maintained

The objection to the specification for the use of the trademark TWEEN is maintained for the reasons set forth in the previous office action. Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Claim Rejections Withdrawn

The rejection of claims 3, 5, 7-9, and 13 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "preferably," is withdrawn in light of applicant's amendment thereto.

The rejection of claim 6 under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for the limitation "further controls" in line 2, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 7 under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for the limitation "one control" in line 2, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 8 under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for the limitation "one control" in line 2, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 11 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "the carrier is designed as a test strip," is withdrawn in light of applicant's amendment thereto..

The rejection of claim 12 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the phrase "the carrier is designed as an immunoblot," is withdrawn in light of applicant's amendment thereto.

The rejection of claim 13 under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for the limitation "the VDRL antigen bands" in line 2, is withdrawn in light of applicant's amendment thereto.

The rejection of claim 19 under 35 U.S.C. 112, second paragraph, because there is insufficient antecedent basis for the limitation "the detection method" in line 3, is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claim 13 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained for the reasons set forth in the previous office action. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues:

1. That the claimed subject matter is clearly described in the specification at, for example, page 7. Applicant asserts that Figures 4 and 5 depict a carrier that allows detection of IgG and IgM antibody classes.

2. That the examiner's allegation that various immunoassay steps are required to differentiate between IgG and IgM antibodies may be untrue and does not support a written description rejection if it is. Applicant asserts that the examiner has conceded that the carrier described in the application allows the user to differentiate between IgG and IgM using standard techniques, so the rejection should be withdrawn.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, as stated previously, neither the specification nor the art show any VDRL antigen that allows said differentiation. Page 7 of the instant specification simply states that the carrier allows differentiation between IgG and IgM. This is not a description of anything and does not overcome the scientific reasoning set forth previously. Figures 4 and 5 do not show a carrier that has differentiated anything. In Figures 4 and 5, the carrier was incubated with anti-human IgG and IgM antibodies conjugated to alkaline phosphatase and later with a chromogen/substrate solution (see specification, page 11 and 12). Without these additional

reagents, the carrier itself would have shown no color and would not have allowed differentiation of anything.

Regarding argument 2, it is noted that applicant has provided neither evidence or even any scientific reasoning to show that the examiner's statements are untrue. Further, the examiner has not conceded that the carrier allows the user to differentiate between IgG and IgM. As stated previously, it is the other reagents that are not included in the carrier that allow differentiation. Neither the specification nor the art has shown any VDRL antigen that allows said differentiation.

As outlined previously, the instant claim is drawn to a carrier for diagnosis and/or follow-up of a Treponema infection comprising at least one immobilized cardiolipin and at lease one immobilized Treponema-specific antigen. Said carrier is characterized in that the VDRL antigen bands allow a differentiation between anti-VDRL-IgG and anti-VDRL-IgM antibodies after reaction with a patient's sample.

The specification discloses an immunochromatographic test strip test where the VDRL antigen, as well as several other Treponema-specific antigens have been applied to nitrocellulose. In the examples, the test strip is contacted with patient serum, allowing any antibodies present in said serum to bind to the antigens on the test strip. Bound antibodies are then visualized by exposing the strip to anti-human IgG, IgM, or IgA antibodies conjugated with alkaline phosphatase. Colored substrate for alkaline phosphatase is added, and color can be seen where the antibody conjugate has bound to serum antibodies, which in turn, have bound to the antigen on the test strip. This type of sandwich immunoassay is standard in the art (see for example, Sambri *et al.*, Clin. Diag. Lab. Immunol., 8:534-539, 2001, IDS filed 4/20/2006).

In the described method, it is the addition of either anti-human IgG or IgM that allows differentiation between anti-VDRL IgG and IgM antibodies in the patient sample. Neither the specification, nor the art show any VDRL antigen that allows said differentiation. To do so, the VDRL would have to have immunoglobulin class-specific binding, and this has not been shown. Therefore, the specification does not provide written description for any antigen meeting the limitations of claim 13.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-6, 10-11, 19, and newly submitted claims 21 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over West *et al.* (Sex. Transm. Inf., 78:282-285, Aug. 2002) in view of Egglestone *et al.* (Communicable Dis. Pub. Health, 3:15-162, 2000), for the reasons set forth in the previous office action.

Applicant argues:

1. That the RPR test does not employ a carrier. Applicant refers to the IMMUTREP RPR product sheet and the BD RPR test product sheet to show that the RPR test contains VDRL antigen particles in suspension with charcoal particles.

2. That binding the labile structure of cardiolipin to a carrier while maintaining its reactivity to anti-cardiolipin antibodies is not trivial and is not taught by West.

3. That the Egglestone reference does not suggest creating a single carrier comprising both immobilized cardiolipin and immobilized Treponema-specific 47 kD antigen.

4. That the Egglestone reference teaches away from the instant invention because the reference suggests multiple, separate assays.

5. That one would not be motivated to combine the RPR and RST tests because the assays require different test procedures, different storage, different conservation substances, and the like. Applicant asserts that applying cardiolipin antigen and Treponema antigen on a single carrier, while allowing both antigens to be processed in such a way as to allow anti-Treponema antibody detection and anti-cardiolipin detection is not trivial. Applicant refers to the appendix submitted with their remarks to show that the conditions suitable for detection of VDRL bands are not suitable for detection of Treponema bands. Said appendix shows an immunoblot where the concentration of TWEEN is 0.01%, which shows a positive result for VDRL, and an immunoblot where the concentration of TWEEN is 0.05%, which shows a negative result for

VDRL. Applicant asserts that "only under particular conditions do both VDRL and Treponema-specific antigens reliably show reactivity."

6. That neither reference suggests a spatial resolution of both antigens.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, The Omega insert states "IMMUTREP RPR is a modified form of IMMUTREP VDRL ANTIGEN which contains carbon particles to improve the visual reading of the result." This statement specifically says that the IMMUTREP VDRL antigen contains carbon particles. The BD RPR test insert states that the "RPR Card antigen suspension is a carbon particle cardiolipin antigen." One does not generally refer to *an* antigen when they are referring to multiple molecules that are simply in suspension with each other. Furthermore, product inserts from other companies bear out the fact that the RPR test contains immobilized cardiolipin. The ASI RPR test card product insert states, "the reagin-type antibody binds with the antigen that is composed of a complex of cardiolipin, lecithin and cholesterol particles with activated charcoal" (see section 3, Principle of the Procedure). The product insert from Weiner Labs RPR test states, "In the rapid test for plasmatic reagins (RPR) the "reagins" present in individuals infected with *T. pallidum* are detected by their reaction to a cardiolipin antigen, lecithin and cholesterol adsorbed onto charcoal particles" (under PRINCIPLE, page 1). However, even if the cardiolipin were not bound to the charcoal before mixing the particles in suspension, charcoal is known to adsorb cardiolipin, lecithin, and cholesterol. Mixing VDRL antigen in suspension with charcoal particles would result in VDRL that is adsorbed to the charcoal. Finally, the invention that is made obvious by the cited references is not cardiolipin bound to charcoal. According to the invention, the VDRL and Treponema-specific antigens are bound to a test strip. The obviousness of this is not negated by whether or not the RPR contains VDRL bound to charcoal.

Regarding argument 2, arguments of counsel cannot take the place of factually supported objective evidence. In fact, the specification and the breadth of the claims suggest the opposite of what applicant is arguing. The claims do not require any special treatment or conditions for the antigens to be bound to the carrier and the specification does not mention any difficulties one of skill in the art might encounter. In the specification, the non-trivial method used to bind the VDRL to the carrier was to drip the antigen solution onto the carrier. Furthermore, binding of

cardiolipin to a carrier was known in the art prior to applicant's invention, even as far back as 1987. Pederson *et al.* (J. Clin. Microbiol., 25:1711-1716, 1987) and WO 91/10138 were submitted by applicant in the Information Disclosure Statement, filed on 4/20/2006. Both of these show binding of cardiolipin to a carrier. Without any evidence to the contrary, one must conclude that one of ordinary skill in the art would have been aware of the ways that cardiolipins could have been bound to a carrier.

Regarding arguments 3 and 6, the test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art. While Egglestone does not specifically suggest creating a single carrier comprising both immobilized cardiolipin and immobilized Treponema-specific 47 kD antigen, this does not mean that the rejection is inappropriate. The focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge. This is so regardless of whether the source of that knowledge and ability was documentary prior art, general knowledge in the art, or common sense. As set forth previously, immunochromatographic test strips were known in the art and both the VDRL and 47 kD antigen were known and had been used separately bound to carriers. Combining them onto a single test strip would have been simply combining known elements with a predictable result. Furthermore, it was suggested in the art that tests for both non-treponemal antigens as well as for treponemal antigens should be used in the diagnosis of syphilis.

Regarding argument 4, the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed. *In re Fulton* 391 F.3d at 1200-01, 73 USPQ2d at 1145-46.

Regarding argument 5, as stated previously, arguments of counsel cannot take the place of factually supported objective evidence. The specification and the breadth of the claims suggest the opposite of what applicant is arguing. The claims do not require any special treatment or conditions necessary for the carrier to work and the specification does not mention any difficulties one of skill in the art might encounter. It is of note that applicant is arguing that for the carrier to work, the concentration of TWEEN must be well below 0.05%. However, in

the examples provided in the specification, a concentration of 0.4% was used. As the specification lacks any teaching that the TWEEN concentration is important, and as the carrier worked at both a very low concentration and at a concentration much higher than that normally used in immunoassays, the two immunoblots submitted by applicant with no corresponding information regarding the experimental conditions and no explanation as to why these teachings are at odds with the specification, and as immunoblots using both VDRL and the 47 kD antigen were known in the art, one would expect that those of ordinary skill in the art easily have determined the required conditions for operability of a carrier containing both types of antigens.

As outlined previously, the instant claims are drawn to a carrier for diagnosis and/or follow-up of a Treponema infection, comprising a) at least one immobilized cardiolipin and b) at least one immobilized Treponema-specific antigen (claim 1); characterized in that the cardiolipin is present together with lecithin and cholesterol as VDRL antigen, said products being preferably present in a mass ratio of cardiolipin:lecithin:cholesterol of 0.1-4.0:1-5.0:1-10 (claims 2 and 21); characterized in that the antigens are selected from Treponema pallidum-specific antigen, preferably the 15 kD, 17 kD, 44.5 kD and 47 kD antigen (claims 5 and 26); characterized in that the carrier comprises further controls (claim 6); characterized in that the carrier is selected from nitrocellulose, PVDF (polyvinylidene difluoride), nylon, cellulose acetate, polystyrene (claim 10); characterized in that the carrier is designed as a test strip for use in immunodiagnostics (claim 11); characterized in that the VDRL antigen bands applied to the carrier allow a differentiation between anti-VDRL-IgG and anti-VDRL-IgM antibodies after reaction with a patient's sample, preferably selected from blood, serum, plasma, liquor or synovial fluid (claim 13); and to a test kit for the diagnosis of a Treponema infection and/or the follow-up of a Treponema infection, comprising a carrier according to claim 1 and further reagents as well as an instruction manual (claim 19).

West *et al.* disclose two tests for the detection of syphilis, the RPR test and RST (see abstract). As evidenced by the RPR product information sheets from Omega Diagnostics (Omega Diagnostics Ltd., IMMUTREP RPR product sheet) and Becton, Dickinson, and Company (BD Macro-Vue RPR Card Tests), the RPR test is an agglutination test where VDRL antigen (cardiolipin, lecithin, and cholesterol) is immobilized on carbon particles (a carrier). The RST is a immunochromatographic strip test that contains the 47 kD *Treponema pallidum* antigen

immobilized in a line on a test strip (carrier), as well as a control line (see page 282, column 1, paragraph 1 and page 282, column 2, paragraph 3).

West *et al.* differs from the instant invention in that the VDRL antigen and the 47 kD antigen are not immobilized on a single carrier, the control is not disclosed as a serum or cut-off control, and the carrier material is not disclosed as nitrocellulose, PVDF, nylone, cellulose, acetate, or polystyrene. The test is also not specifically disclosed as containing instructions for use.

Egglestone *et al.* disclose recommendations for serological diagnosis of syphilis. Egglestone *et al.* disclose using a combination of a quantitative non-treponemal test (such as the VDRL and RPR tests, which use cardiolipin antigens) with a specific treponemal immunoassay (see page 159, column 2). Egglestone *et al.* states that combining the non-treponemal test with an assay for specific anti-treponemal IgM helps to assess the stage of infection and provide a baseline for monitoring treatment (see page 160, column 2, paragraph 3). Egglestone *et al.* specifically recommend combining a treponemal immunoassay (for IgM, IgG, or both) with a non-treponemal test (see page 162, recommendation 3).

Therefore, it would have been obvious to one of skill in the art, at the time of invention, to use the VDRL antigen (as disclosed by West *et al.* and Egglestone *et al.*) on the immunochromatographic test strip disclosed by West *et al.*, thus combining the two tests into one, for ease of use and because Egglestone *et al.* recommends using both tests in the diagnosis of syphilis. It would also have been obvious to use nitrocellulose, PVDF, nylone, cellulose, acetate, or polystyrene as the strip material because immunochromatographic test strips are common in the art and these materials are the standard materials in such strips.

One would have had a reasonable expectation of success because immunochromatographic tests performed using test strips are commonly used in the art with numerous different antigens. Further, immunoassays using VDRL antigen and the 47 kD treponemal antigen have been shown to be successful by West *et al.*

With regard to claim 19, according to MPEP 2112.01, Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004).

Claims 1-3, 5-12, 19, and newly submitted claims 21-23 and 26-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zarakolu *et al.* (J. Clin. Microbiol., 40:3064-6065, Aug. 2002) in view of Sambri *et al.* (Clin. Diag. Lab. Immunol., 8:534-539, 2001) for the reasons set forth in the previous office action.

Applicant argues:

1. That the Zarakolu reference merely represents a first success in providing a test strop system suitable for detecting Treponema infection. Applicant argues that the reference only employs one Treponema antigen.

2. That the test strip taught by Sambri only contains Treponema antigens.

3. That the there is no suggestion in either Zarakolu or Sambri to combine different kinds of molecules (such as cardiolipin and Treponema antigens) on a single carrier.

4. That it would not be apparent that a carrier comprising both types of antigens would be functional or easy to use. Applicant argues that creating an assay that allows Treponema and non-Treponema antigens to be processed and detected is not trivial and it was not predictable that detection of these antigens could be achieved using a single carrier.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding arguments 1 and 2, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Regarding argument 3, the prior art reference (or references when combined) need not teach or suggest all the claim limitations. The focus when making a determination of obviousness should be on what a person of ordinary skill in the pertinent art would have known at the time of the invention, and on what such a person would have reasonably expected to have been able to do in view of that knowledge. This is so regardless of whether the source of that knowledge and ability was documentary prior art, general knowledge in the art, or common sense. As set forth previously, immunochromatographic test strips were known in the art and both the VDRL and 47 kD antigen were known and had been used separately bound to carriers. Combining them onto a single test strip would have been simply combining known elements

with a predictable result. Furthermore, it was suggested in the art that tests for both non-treponemal antigens as well as for treponemal antigens should be used in the diagnosis of syphilis.

Regarding argument 4, arguments of counsel cannot take the place of factually supported objective evidence. In fact, the specification and the breadth of the claims suggest the opposite of what applicant is arguing. The claims do not require any special treatment or conditions necessary for the carrier to work and the specification does not mention any difficulties one of skill in the art might encounter. As immunoblots using both VDRL and the 47 kD antigen were known in the art, one would expect that those of ordinary skill in the art easily have determined the required conditions for operability of a carrier containing both types of antigens, absent any evidence to the contrary.

As outlined previously, the instant claims are drawn to a carrier for diagnosis and/or follow-up of a Treponema infection, comprising a) at least one immobilized cardiolipin and b) at least one immobilized Treponema-specific antigen (claim 1); characterized in that the cardiolipin is present together with lecithin and cholesterol as VDRL antigen, said products being preferably present in a mass ratio of cardiolipin:lecithin:cholesterol of 0.1-4.0:1-5.0:1-10 (claims 2 and 21); characterized in that the cardiolipin is present in at least two, preferably at least three, particularly preferably at least four different concentrations at different positions of the carrier (claim 3); characterized in that the antigens are selected from Treponema pallidum-specific antigen, preferably the 15 kD, 17 kD, 44.5 kD and 47 kD antigen (claims 5 and 26); characterized in that the carrier comprises further controls (claim 6); characterized in that one control is a serum control, protein A (claims 7 and 27); characterized in that one control is a cut-off control, comprising purified human immunoglobulin (claims 8 and 28); characterized in that it comprises a serum control which comprises protein A and a cut-off control which comprises human immunoglobulin (claims 9 and 29); characterized in that the carrier is selected from nitrocellulose, PVDF (polyvinylidene difluoride), nylon, cellulose acetate, polystyrene (claim 10); characterized in that the carrier is designed as a test strip for use in immunodiagnostics (claim 11); characterized in that the carrier is designed as an immunoblot (claim 12); characterized in that the VDRL antigen bands applied to the carrier allow a differentiation between anti-VDRL-IgG and anti-VDRL-IgM antibodies after reaction with a patient's sample,

preferably selected from blood, serum, plasma, liquor or synovial fluid (claims 13 and 30); and to a test kit for the diagnosis of a Treponema infection and/or the follow-up of a Treponema infection, comprising a carrier according to claim 1 and further reagents as well as an instruction manual (claim 19).

Zarakolu *et al.* disclose an immunochromatographic test strip where the 47 kD treponemal antigen has been immobilized in a thin line on nitrocellulose strips. The strips also contain a line of anti-human IgG to serve as a control (see page 3064, column 2, paragraph 2). The line of anti-human IgG would serve as both a serum control and as a cut-off control, as it would indicate the presence of serum and immunoglobulins. Zarakolu *et al.* also disclose the RPR test and disclose that syphilis testing is usually a two step procedure where non-treponemal tests (such as RPR) are used in combination with specific tests for treponemal antigens (see page 3064, column 1, paragraph 1).

Zarakolu *et al.* differ from the instant claims in that the VDRL antigen is not disclosed on the same carrier as the 47 kD antigen, the VDRL antigen is not present in at least two concentrations at different positions of the carrier, the test is not disclosed as having been designed as an immunoblot, and the test is not disclosed as containing instructions for use.

Sambri *et al.* disclose a Western blot test where test strips were created with different antigens in different positions on nitrocellulose strips (see page 535, column 2, paragraphs 2-3).

Therefore, it would have been obvious to one of skill in the art, at the time of invention, to use the VDRL antigen on the immunochromatographic test strip disclosed by Zarakolu *et al.*, thus combining the two tests into one, for ease of use and because both tests are generally used in the diagnosis of syphilis. Additionally, according to the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it is obvious to substitute one known component for another where one of ordinary skill in the art could have substituted one known element for another, and the results would have been predictable. Thus, it would have been obvious to use multiple concentrations of VDRL antigen in different positions on the test strip of either Zarakolu *et al.* or Sambri *et al.* instead of multiple treponemal antigens because one would achieve predictable results.

One would have had a reasonable expectation of success because immunochromatographic tests performed using test strips are commonly used in the art with

numerous different antigens (as evidenced by Sambri *et al.*). Further, immunoassays using VDRL antigen and the 47 kD treponemal antigen have been shown to be successful by Zarakolu *et al.*

With regard to claim 19, according to MPEP 2112.01, Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the limitation "the cardiolipin:lecithin:cholesterol" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley or Robert Mondesi can be reached at 571-272-0898 or 571-272-0956, respectively. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Shanon A. Foley/
Supervisory Patent Examiner, Art Unit 1645